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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,501	12/17/2001	Guido Henning	Le A 35 012	4394

7590 03/08/2006

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EXAMINER	
CROSS, LATOYA I	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,501	HENNING ET AL.	
	Examiner	Art Unit	
	LaToya C. Younger	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 19, 2005 has been entered. Claims 1-5 and 7 are pending.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Journal article "Single Cell Multiple Biomarker Analysis in Archival Breast Fine-Needle Aspiration Specimens: Quantitative Fluorescence Image Analysis of DNA Content, p53 and G-actin as Breast Caner Biomarkers" by Rao et al.

Rao et al teach a method for evaluating breast legions for cancerous cells. The method of Rao et al involves staining breast legion samples with stain and biomarkers, such as p53, G-actin and DNA content. In the abstract of the article, Rao et al specifically teach QF image analysis of multiple biomarkers (p53, G-actin and DNA content) on a single cell basis. With respect to the staining, Rao et al teach at page 1028 that immunofluorescent labeling takes place by using a Code-On automatic stainer. Page 1030 further describes the staining as distinctive in that G-actin stains more intensively in

cytoplasm, whereas p53 is slightly stronger in the nuclei of tumor cells. After staining, the samples are scanned by an automated image analysis system and biomarkers are detected. Cellular portions of the samples are imaged and measured, and the values are automatically stored in a database. See page 1028. The data is analyzed quantitatively and qualitatively and the results are converted into positive-negative schema. The data analyses are carried out using a software program (Microsoft Excel program). The image analysis system is considered to be an automatic information processing system that is linked to a diagnostic expert system. The software program taught by Rao et al is taken to be a diagnostic expert system because of its ability to convert the quantitative values into positive-negative schema (i.e. convert the data into an diagnosis of a disease state). See page 1028, 1030. Rao et al further performed the method using multiple markers, such the combination of G-actin and DNA content. The articles states that none of the benign cases were positive for G-actin and DNA simultaneously, and that none of the cancer cases were negative for G-actin and DNA simultaneously. Thus, the measurement of the two biomarkers took place simultaneously as a mixture of biomarkers. The article teaches that using multiple markers provides a powerful tool for breast cancer detection. See page 1031. With respect to claim 5, Rao et al's teaching of the detection of cancerous cells in breast legions meet the limitation of detecting tumors in the mammary gland.

4. Claims 1, 3, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 6,007,996 to McNamara et al.

McNamara et al teach a method for analyzing cells for the detection of cancerous cells, such as those found in breast cancer, ovarian and/or endometrial cancer and prostate cancer. The method of McNamara et al involves staining the cell sample with multiple stains including immunohistochemical, histological and DNA ploidy stains. Each immunohistochemical stain is coupled

with a primary antibody known to bind with their respective cytological markers and are used in diagnosis of diseases, such as cancer. Specifically, McNamara et al teach antibodies p53, Her-2/neu, EGFR, Ki-67 and Bcl-2 (col. 40, lines 25-67). For breast cancer, McNamara et al teach using PR, Her-2/neu, p53, CD31 and Ki-67. For prostate cancer, McNamara et al teach using Ki-67, CD31 and p53 (col. 41, lines 28-40). At col. 41, lines 55-64, McNamara et al teach that a clinician can simultaneously detect multiple cytological markers (p53, Her-2/neu, Ki-67) allowing more accurate diagnosis. After staining of the samples, spectral imaging is performed and the data is collected using a SPECTRACUBE ™ (col. 36, line 63 – col. 37, line 23). In analyzing the results of the data collected, McNamara et al teach using spectral and spatial data. The spectral data is displayed as a useful image for the user. The spatial-spectral correlation of the spectrum image provides data about various types of cells that may appear similar to the naked eye. Thus, in addition to the image data, the cells can also be differentiated.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Rao et al or McNamara et al in view of US Patent 5,109,429 to Bacus et al.

The disclosures of both Rao et al and McNamara et al are described above. Neither reference teaches a kit having the necessary reagents for carrying out the method for detecting cancerous cells.

Bacus et al teach a kit for analyzing biological specimens for cancer diagnosis and/or prognosis. The kit of Bacus et al comprises slides, one or more bottles of staining reagent, auxiliary agents, such as sulfonating agents and buffer, instructions for the operator and a reference area for calibration. Bacus et al teach that the kit provides an easy and inexpensive means for detecting minute alterations in specimen cells. It would have been obvious to one of ordinary skill in the art to incorporate the components needed to carry out the methods of Rao et al or McNamara et al into a kit to allow a user to have all the supplies needed for easy detection of cancer cells in convenient package.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 2 and 4-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6, 9 and 10 of copending Application No. 10/022,618. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are broader than those of the 10/022,618 application in that the instant claims recite cancer cells and their precursors, whereas the claims of the '618 application recite cancer cells and their precursors "in uterine cervical smears". Instant claim 1 recites and "automatable" method, wherein the signal intensities are combined and accredited, which limitations are recited in claim 9 of the '618 application. The instant claims are broader than the claims of the '618 application and are thus anticipated by the '618 application. See *In re Goodman*.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Applicants may file a Terminal Disclaimer to overcome this provisional double patenting rejection.

Response to Arguments

6. Applicant's arguments filed March 31, 2005 have been fully considered but they are not persuasive.

With respect to the anticipation rejection over Rao et al, Applicants argue that Rao et al fail to teach simultaneously detecting signal intensities of color mixtures resulting from the markers and combining and accrediting the signal intensities. At the first full paragraph of page 1028, Rao et al teach that multiple biomarkers are evaluated simultaneously. After staining, the samples are scanned by an automated image analysis system and biomarkers are detected. Further, at page 1031, Rao

et al teach that the analysis showed that none of the results were positive or negative for G-actin and DNA content simultaneously.

Applicants further argue that the Rao et al reference fails to teach single cell analysis. However, in the abstract of the reference, the authors mention QF image analysis simultaneously on a single cell basis.

With respect to the McNamara et al rejection, Applicants again argue that McNamara et al fail to teach simultaneously detecting signal intensities of color mixtures resulting from the markers and combining and accrediting the signal intensities. The method of McNamara et al involves staining the cell sample with multiple stains including immunohistochemical, histological and DNA ploidy stains. Each immunohistochemical stain is coupled with a primary antibody known to bind with their respective cytological markers. At col. 41, lines 55-64, McNamara et al teach that a clinician can simultaneously detect multiple cytological markers (p53, Her-2/neu, Ki-67) allowing more accurate diagnosis.

With respect to whether McNamara et al teach single cell analysis, the Examiner points out that the reference teaches cell differentiation, which implies differentiating single cells.

The Examiner notes Applicants' request to hold remarks regarding the obviousness double patenting rejection in abeyance until claims are allowable in the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LaToya C. Younger whose telephone number is 571-272-1256. The examiner can normally be reached on Monday-Friday 10:30 a.m. - 8:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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